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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,897	09/22/2006	Peter Wisdom Atadja	33310A	7190

1095 7590 10/19/2010

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 101/2
EAST HANOVER, NJ 07936-1080

EXAMINER	
PURDY, KYLE A	

ART UNIT	PAPER NUMBER
1611	

MAIL DATE	DELIVERY MODE
10/19/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,897	ATADJA ET AL.	
	Examiner	Art Unit	
	Kyle Purdy	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the amendments filed on 07/09/2009 wherein claims 1, 2, 4-14 and 21-24 have been cancelled and claim 25 is newly added.

2. Claim 25 is presented for examination on the merits. The following rejections are made.

Response to Applicants' Arguments

3. Applicants arguments filed 07/09/2009 regarding the rejection of claim 1, 2 and 4-14 made by the Examiner under 35 USC 112, first paragraph (written description) have been fully considered and they are found persuasive. This rejection has been overcome by cancellation of the claims.

4. Applicants arguments filed 07/09/2009 regarding the rejection of claim 1, 2, 4-14 and 24 made by the Examiner under 35 USC 103(a) over Remiszewski et al. (US 6552065) in view of Verner et al. (US 7276612) and Griffin et al. (US 2005/0020570) have been fully considered and they are found persuasive. This rejection has been overcome by cancellation of the claims.

New Rejections, Necessitated by Amendment
Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. **Claim 24 is rejected under 103(a) as being unpatentable over Remiszewski et al. (US 6552065; of record) in view of Verner et al. (US 7276612; of record) and Griffin et al. (US 2005/0020570; of record).**

9. Remiszewski teaches hydroxamate HDA inhibitor compounds that possess anti-prolfierative properties and have been studied for their therapeutic effects on cancer cells, (abstract; column 1, lines 14-40, Example P3; see also column115-116, **Compound 200** = N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2-E-2-propenamide). Remiszewksi teaches that HAD inhibtors are useful for treating a proliferative disease may

furthermore by a hyperproliferative condition such as **leukemias**, hyperplasias, fibrosis and angiogenesis (see column 22, lines 10-40).

10. Although Remiszewski suggest treating leukemia with N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2-E-2-propenamide, Remiszweski does specifically teach AML. Further, Remiszewski does not teach the instantly claimed combination of an HDAI and an FLT-3 inhibitor (i.e. Midostaurin).

11. Verner teaches that HDAIs are useful for treating various conditions, including AML, and may be co-administered with other therapeutic agents to treat said conditions (column 49, line 20-35; column 50, line 62 to column 51, line 15). Verner does not specifically teach the instant claimed combination of a HDAI and a FLT-3 inhibitor (e.g. Midostaurin) for treating AML.

12. Griffin teaches that aberrant expression of the FLT3 gene has been documented in both adult and childhood leukemias, including **acute myeloid leukemia (AML)**, AML with trilineage myelodysplasia (AMLUTMDS), acute lymphoblastic leukemia (ALL), and myelodysplastic syndrome (MDS)(see [0252]). Griffin teaches that **Midostaurin (or PKC42)** possesses FLT-3 inhibitory properties that render it particularly useful as an inhibitor of FLT-3 receptors and especially in the treatment of leukemias and myelodysplastic syndromes (see [0232]-[0235]).

13. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Remiszewski, Verner and Griffin with a reasonable expectation for success in arriving at a method of treating AML by administering an FLT-3 inhibitor (e.g. Midostaurin) as taught by Griffin and a HDAI (e.g. N-hydroxy-3-[4-[[[2-(2-methyl-1H-indol-3-yl)-ethyl]-amino]methyl]phenyl]-2-E-2-propenamide) as taught by

Remiszewski for treating AML. One would have been motivated to do so because Vernier suggests that HDAIs may be combined with other agents to treat AML and therefore one would have combined an HDAI (e.g. Compound 200) as taught by Remiszewski with another agent such as an FLT-3 inhibitor (e.g. Midostaurin) as taught by Griffin to treat AML since both classes of drugs are used to treat AML, as evidenced by the teaching of Vernier and Griffin. ((Cf. In re Kerkhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980). Besides, Griffin teach that AML is associated with deregulated FLT-3 and therefore one would expect that the combination of an HDAI (e.g. Compound 200) as taught by Remiszewski with an FLT-3 inhibitor (e.g. Midostaurin) as taught by Griffin would also be effective in treating AML. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

15. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

17. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Kyle Purdy/
Examiner, Art Unit 1611
October 14, 2010

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611